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10/588,978	04/24/2007	Geoffrey Gerard Hayes	Y2440-00004	4150

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EXAMINER	
BROWE, DAVID	
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1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,978	HAYES ET AL.	
	Examiner	Art Unit	
	DAVID M. BROWE	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *138-140,142-162 and 164-210* is/are pending in the application.

4a) Of the above claim(s) *190-210* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *138-140,142-162 and 164-189* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *February 3, 2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 138-140, 142-162, 164-210 are pending; claims 141 and 163 are cancelled.

Applicants timely submission of amendments and arguments in the reply filed February 3, 2010 in response to the First Office Action on the Merits is acknowledged.

Election/Restrictions

A). Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 138-140, 142-162, and 164-189, drawn to a unit dose of a controlled-release pharmaceutical formulation, wherein said formulation includes melt-extruded multiparticulates or granulates, comprising a rubbery matrix including a neutral poly(ethyl acrylate, methyl methacrylate) copolymer and an active agent, classified in class 424, subclass 487.

II. Claims 190-210, drawn to methods of preparing and imparting a tamper resistance to a tamper-resistant, controlled-release pharmaceutical formulation, classified in class 514, subclass 781.

Inventions I and II are related as product made and process of making. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the product as claimed can be made by another and materially different process, such as co-precipitation without the incorporation of ethyl cellulose and an opiod antagonist, resulting in a unit dose that is not tamper resistant.

Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art in view of their different classification;

(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

(d) the prior art applicable to one invention would not likely be applicable to another invention;

(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

B). Newly submitted claims 190-210 are directed to inventions that are independent or distinct from the invention originally claimed for the following reasons: newly added claims 190-210, drawn to methods of making and imparting a tamper-resistance to a controlled-release pharmaceutical formulation, represent a different statutory class of invention and fall into a different classification.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for

prosecution on the merits. Accordingly, claims 190-210 are hereby withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Withdrawal of Prior Claim Rejections - 35 USC § 103

Applicant's arguments filed February 3, 2010 have been fully considered and are persuasive. Therefore, the 35 USC § 103 rejection of claims 138-164 presented in the First Office Action is hereby withdrawn. Upon further search and consideration, however, a new grounds of rejection is being made herein below.

Accordingly, this action is non-final.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 102(b)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 138-140, 142-144, 151, 153, 165-170, 177, and 179 are rejected under 35 U.S.C. 102(b) as being anticipated by Wright, IV *et al.* (U.S. Patent Application Pub. No. 2003/0044458).

Wright, IV *et al.* disclose a controlled-release unit dose of melt-extruded multi-particulates or granulates having a rubbery matrix comprising a neutral poly(ethyl acrylate, methyl methacrylate) copolymer and an active agent (Pg. 1, secs. 0002; Pg. 3, secs. 0030, 0033, 0036-0038; Pg. 4, secs. 0039-0043; Pg. 6, secs. 0065-0067; Pg. 7,

sec. 0074; Pg. 8, secs. 0082-0088; Pg. 9, secs. 0089, 0092, 0094). The neutral poly(ethyl acrylate, methyl methacrylate) copolymer is Eudragit NE 30 D (Pg. 9, sec. 0089). The active agent is oxycodone or a pharmaceutically acceptable salt thereof (Pg. 3, sec. 0037); or can be another opioid, a stimulant, a barbiturate, an anti-depressant, a dissociative anesthetic, or combinations thereof (Pg. 3, secs. 0033, 0036-0038; Pg. 4, secs. 0039-0043). Oxycodone can be in combination with naltrexone or another opioid antagonist (Pg. 1, secs. 0002, 0007-0009; Pg. 2, sec. 0029; Pg. 3, sec. 0037; Pg. 4, sec. 0046; Pg. 9, sec. 0098; Pg. 10, secs. 0101, 0104; Pg. 11, sec. 0115). The controlled-release matrix includes one or a combination of ethylcellulose, a water-insoluble ammonium methacrylate copolymer, and at least one other release-modifying polymer (Pg. 7, sec. 0071; Pg. 8, secs. 0084-0086, 0088; Pg. 9, sec. 0089).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 138-140, 142-162, and 164-189 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wright, IV *et al.* (U.S. Patent Application Pub. No. 2003/0044458), in view of Oshlack *et al.* (U.S. Patent No. 5,958,452) and Oshlack *et al.* (U.S. Patent Application Pub. No. 2002/0010127).

Applicant Claims

Applicants claim a controlled-release unit dose of melt-extruded multi-particulates or granulates having a rubbery matrix comprising a neutral poly(ethyl acrylate, methyl methacrylate) copolymer and an active agent. The active agent is oxycodone or a pharmaceutically acceptable salt thereof; or can be another opioid, a stimulant, a barbiturate, an anti-depressant, a dissociative anesthetic, or combinations thereof. Oxycodone is present in an amount from 5-160 mg, and can be in combination with naltrexone or another opioid antagonist in individual or separate multi-particulates. The controlled-release matrix includes one or a combination of ethylcellulose, a water-insoluble ammonium methacrylate copolymer, and at least one other release-modifying

polymer. The matrix can further include a plasticizer and a bulking agent. The controlled-release unit dose is formulated for once or twice a day dosing; and contains up to 60 wt% active agent, 15-50 wt% neutral poly(ethyl acrylate, methyl methacrylate) copolymer, 10-50 wt% ethylcellulose, 5-60 wt% insoluble ammonium methacrylate copolymer, and 7.5-20 wt% plasticizer. Controlled-release unit doses containing oxycodone can be specifically formulated to exhibit desired *in vitro* oxycodone dissolution rates; as assessed by standard USP Paddle or Basket Methods at 100 rpm, 900 ml aqueous buffer, pH 1.2 or 1.6-7.2, and 37ºC; and to deliver the peak plasma level of oxycodone *in vivo* at 2-17 hours after administration of the dosage form.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Wright, IV *et al.* disclose a controlled-release unit dose of melt-extruded multi-particulates or granulates having a rubbery matrix comprising a neutral poly(ethyl acrylate, methyl methacrylate) copolymer and an active agent (Pg. 1, secs. 0002; Pg. 3, secs. 0030, 0033, 0036-0038; Pg. 4, secs. 0039-0043; Pg. 6, secs. 0065-0067; Pg. 7, sec. 0074; Pg. 8, secs. 0082-0088; Pg. 9, secs. 0089, 0092, 0094). The neutral poly(ethyl acrylate, methyl methacrylate) copolymer is Eudragit NE 30 D (Pg. 9, sec. 0089). The active agent is oxycodone or a pharmaceutically acceptable salt thereof (Pg. 3, sec. 0037); or can be another opioid, a stimulant, a barbiturate, an anti-depressant, a dissociative anesthetic, or combinations thereof (Pg. 3, secs. 0033, 0036-0038; Pg. 4, secs. 0039-0043). Oxycodone is present in an amount from 5-160 mg, and can be in combination with naltrexone or another opioid antagonist in individual or separate multi-particulates (Pg. 1, secs. 0002, 0007-0009; Pg. 2, sec. 0029; Pg. 3, sec. 0037; Pg. 4,

sec. 0046; Pg. 9, sec. 0098; Pg. 10, secs. 0101, 0104; Pg. 11, sec. 0115). The controlled-release matrix includes one or a combination of ethylcellulose, a water-insoluble ammonium methacrylate copolymer, and at least one other release-modifying polymer (Pg. 7, sec. 0071; Pg. 8, secs. 0084-0086, 0088; Pg. 9, sec. 0089). The controlled-release unit dose affords tamper-resistance (Pg. 1, sec. 0029; Pg. 10, sec. 0100); and can contain up to 60 wt% active agent, 15-50 wt% neutral poly(ethyl acrylate, methyl methacrylate) copolymer, 10-50 wt% ethylcellulose, 5-60 wt% insoluble ammonium methacrylate copolymer, and 7.5-20 wt% plasticizer (Pg. 8, secs. 0085-0086, 0088; Pg. 9, sec. 0089; Pg. 11, sec. 0115).

Oshlack *et al.* (U.S. Patent No. 5,958,452) disclose a controlled-release unit dose matrix comprising a pharmaceutically acceptable acrylic-methacrylic acid copolymer and an active agent (Col. 3, lns. 43-44, 61-65; Col. 4, lns. 5-6, 10-11, 17-20, 31-33; Col. 6, lns. 50-53; Col. 8, lns. 36-39, 43-44, 47-49, 53-56). The active agent can be any water-soluble or water-insoluble drug, and include opioid analgesics, stimulants, hypnotics (which includes barbiturates and dissociative anesthetics), psychotropics (which includes anti-depressants), and sedatives (Col. 6, lns. 50-53, 56-57; Col. 7, lns. 5-8, 9-11, 25). In preferred embodiments, the opioid analgesic is oxycodone in an amount from about 5-400 mg (Col. 7, lns. 35-37, 54-56). The controlled-release matrix can include at least one other release-modifying polymer, such as an alkyl cellulose, particularly ethyl cellulose, or a water-insoluble ammonium methacrylate copolymer (Col. 8, lns. 36-59). The matrix can further include suitable quantities, up to about 50 wt%, of other materials such as plasticizers, lubricants, diluents, binders, and

granulating aids, such as bulking agents (Col. 9, lns. 40-52). The most suitable plasticizer is based on its ability to lower the glass transition temperature (Tg) of the polymer (Col. 6, lns. 30-34), which would impart a rubbery consistency to the controlled-release unit dose matrix in ambient conditions. The matrix may also include retardant materials, such as water-insoluble wax-like thermoplastic substances possibly mixed with one or more wax-like thermoplastic substances that are sparingly water-permeable (Col. 8, lns. 66-67; Col. 9, lns. 1-3), which are known in the art to confer a resistance to *in vitro* extraction of the active agent with common solvents, such as alcohol (Col. 4, lns. 11-16). The controlled-release unit dose can be obtained by melt-extrusion, and formulated as multi-particulate dosage forms suited for once (every 12 hours) or twice (every 24 hours) a day dosing (Col. 3, lns. 50-53, 61-67; Col. 4, lns. 1-3, 5-6, 10, 39-41, 50-53; Col. 11, lns. 61-63). Controlled-release unit doses containing oxycodone can be specifically formulated to exhibit desired *in vitro* oxycodone dissolution rates; as assessed by standard USP Paddle or Basket Methods at 100 rpm, 900 ml aqueous buffer, pH 1.2 or 1.6-7.2, and 37ºC (Col. 9, lns. 44-46; Col. 11, lns. 33-48, 61-67; Col. 12, lns. 1-7, 13-16, 22-27); and to deliver the peak plasma level of oxycodone *in vivo* at 2-17 hours after administration of the dosage form (Col. 12, lns. 9-10, 15-17).

Oshlack *et al.* (U.S. Patent Application Pub. No. 2002/0010127) disclose a controlled-release unit dose matrix comprising a methacrylic acid-ethyl acrylate copolymer and an opioid agonist, such as oxycodone, in combination with an opioid antagonist, such as naltrexone (Pg. 1, sec. 0009, 0011, 0016; Pg. 2, sec. 0018; Pg. 10, sec. 0107; Pg. 13, sec. 0135, 0137; Pg. 14, sec. 0148). The controlled-release matrix

can include at least one other release-modifying polymer, such as an alkyl cellulose, particularly ethyl cellulose, or a water insoluble ammonium methacrylate copolymer (Pg. 13, secs. 0136-0137; Pg. 14, secs. 0144-0145, 0149). The matrix can further include a plasticizer, a lubricant, a granulating aid, such as a bulking agent, and an agent which imparts resistance to active agent extraction by common solvents (Pg. 13, sec. 0140; Pg. 14, secs. 0146, 0151-0152). The controlled-release unit dose can be obtained by melt-extrusion, and formulated as multi-particulate dosage forms suited for once or twice a day dosing (Pg. 2, sec. 0024; Pg. 14, sec. 0149, 0153; Pg. 15, sec. 0156). Controlled-release unit doses containing oxycodone can be specifically formulated to exhibit desired *in vitro* oxycodone dissolution rates; as assessed by standard USP Paddle or Basket Methods at 100 rpm, 900 ml aqueous buffer, pH 1.2 or 1.6-7.2, and 37ºC (Pg. 2, sec. 0023; Pg. 10, sec. 0105; Pg. 13, sec. 0135; Pg. 15, sec. 0162).

Ascertainment of the Difference Between the Scope of the Prior Art and the Claims (MPEP §2141.012)

Wright, IV *et al.* do not explicitly disclose that a controlled-release unit dose of melt-extruded multi-particulates or granulates having a rubbery matrix comprising a neutral poly(ethyl acrylate, methyl methacrylate) copolymer, oxycodone , and naltrexone can be suitable for once or twice a day dosing; can exhibit the specific *in vitro* oxycodone dissolution rates desired; as assessed by standard USP Paddle or Basket Methods at 100 rpm, 900 ml aqueous buffer, pH 1.2 or 1.6-7.2, and 37ºC; and can deliver the peak plasma level of oxycodone *in vivo* at 2-17 hours after administration of the dosage form. These deficiencies are cured by the teachings of Oshlack *et al.* (U.S.

Patent No. 5,958,452) and Oshlack *et al.* (U.S. Patent Application Pub. No. 2002/0010127)

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of the present invention to combine the respective teachings of Wright, IV *et al.*, Oshlack *et al.* (U.S. Patent No. 5,958,452) and Oshlack *et al.* (U.S. Patent Application Pub. No. 2002/0010127) as described *supra* to deduce applicants claimed invention.

Oshlack *et al.* (U.S. Patent No. 5,958,452) and Oshlack *et al.* (U.S. Patent Application Pub. No. 2002/0010127) disclose, as described *supra*, that a controlled-release unit dose matrix comprising any pharmaceutically acceptable acrylate-methacrylate copolymer, ethylcellulose, oxycodone and naltrexone, in the weight percentages claimed, can be suitable for once or twice a day dosing; can exhibit the specific *in vitro* oxycodone dissolution rates desired, as assessed by standard USP Paddle or Basket Methods at 100 rpm, 900 ml aqueous buffer, pH 1.2 or 1.6-7.2, and 37ºC; and can deliver the peak plasma level of oxycodone *in vivo* at 2-17 hours after administration of the dosage form. Since Wright, IV *et al.* disclose that a controlled-release unit dose of melt-extruded multi-particulates or granulates having a rubbery matrix comprises a neutral poly(ethyl acrylate, methyl methacrylate) copolymer, ethyl cellulose, oxycodone, and naltrexone; one of ordinary skill in the art would be motivated to employ the Wright, IV *et al.* formula for a controlled-release unit dose matrix; wherein Eudragit NE 30 D, the neutral poly(ethyl acrylate, methyl methacrylate) copolymer, is

admixed with ethylcellulose, oxycodone and naltrexone in the specified weight percentages; with the reasonable expectation that the resulting controlled-release unit dose will be suitable for once or twice a day dosing; can exhibit the specific *in vitro* oxycodone dissolution rates desired, as assessed by standard USP Paddle or Basket Methods at 100 rpm, 900 ml aqueous buffer, pH 1.2 or 1.6-7.2, and 37ºC; and can deliver the peak plasma level of oxycodone *in vivo* at 2-17 hours after administration of the dosage form.

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DAVID M. BROWE whose telephone number is 571-270-1320. The examiner can normally be reached on Monday-Friday 7:30AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 571-272-0646. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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